

Letter to the Editor

The Territorial Ethics Committee after approval of Italian Law No. 220/2017

Dear Editor,

Ricci et al¹ have debated in their scientific contribution "The National Ethics Committee: a truly valuable asset for clinical trials?" about the connected dilemmas on the adoption of the EU Regulation 536/2014 and about the hypothesis of a National Ethics Committee. The authors have expressed some perplexities regarding several duties that the National Ethics Committee will have, as to express opinions on ethical, scientific and practical aspects related to clinical trials on medicine products for human use conducted by national research centers and university hospitals. Moreover, Ricci et al¹ have highlighted the impossibility that some ethical issues cannot be studied without taking into account their social implications. These and more other issues must be analyzed, for a real guarantee of fundamental rights, only by the Territorial Ethics Committees (TECs) and not by a National Ethics Committee. In the light of these considerations, it is relevant to highlight that the group of Italian bioethics have produced a crucial document, "Carta di Napoli per la Tutela della Persona nelle Sperimentazioni Cliniche"² on the importance of the Ethics Committees as guarantor of patients' safe and fundamental rights.

Recently, the Italian Senate on 22 December 2017 approved the Law No. 220 relating to drug experimentation for human use. In this new Italian law RECs will endure a setback. In particular, the provision in the article 2 of the Italian Law, "National Coordination Center for Territorial Ethics Committees for clinical trials on medicinal products for human use and on medical devices", established the creation of a National Authority for coordination of the TECs on human experimentation for innovative medical drugs for human use into the Italian Agency of Drugs (AIFA). This National Authority will have the scope of coordination, guidance, and monitoring of the activities of evaluation of the ethical aspects related to clinical trials on medicinal products for human use entrusted to the Territorial Ethics Committees.

Since the Institutional Review Boards (IRBs) or Research Ethics Committees (RECs) are in front-line for the protection of human beings enrolled in clinical trials, these bodies have the task of evaluating the proposals of biomedical research projects. In the United States of America (USA), the National Research Act has been repeatedly implemented to form the "Common Rule" which led to the establishment of the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research. The IRBs were the first committees set up in all US offices, where research publicly funded in order to protect the rights of the participants in the trials and to prevent the abuse of science.

Differently from USA, in Italy RECs appeared later, from the mid-80s to the mid-90s. During the years, there was a rapid and sometimes excessive proliferation of them. In the 2011 in Italy, the ECs was a total number of 248.

When the first RECs were created, the reference documents for the evaluation of the research protocols were codes of ethics and medical deontology. The reference to these documents represented the single and essential basis both for the establishment of the RECs and also for the operational phase of evaluation of the experimental protocols. Subsequently, RECs acquired importance and credibility in this role of evaluation of experimentations and became the "tool" to spread and enforce principles and regulations and to advance drug research in our country, like other European and international Countries. Today, the RECs have increasingly specialized in the revision of research's protocol, especially pharmacology innovative protocols.

The Italian National Bioethics Committee (NBC), in the opinions issued during the years related on Ethics Committees, has provided several interesting elements to understand their genesis and development. In the opinion of 2001 on "Guidelines for Ethical Committees in Italy" – the Italian NBC has again highlighted the issues on the matters of the distinction of the ECs and the division of roles, on the definition of skills for the evaluation of clinical trials and welfare practice, on problems nowadays even more intensified by the fact that Ethics Committees are more strongly solicited, also from the legislative point, and mainly engaged in pharmacological experimentation, to the detriment not only of other experimental fields but also of attention to the care practice³.

The Italian Law of 8 November 2012 no. 189 and the subsequent Decree of the Italian Ministry of Health of 8 February 2013 caused a further profound change for the national ECs, requiring a drastic reduction of their number and the establishment of regional ECs, as foreseen in the Articles 10 and 11 (Law 189/2012). Furthermore, the Decree of the Italian Ministry of Health of 8 February 2013 has further defined the functions and criteria for the composition of the Territorial ECs⁴. Even though Italian 2012 Law provided to harmonize some aspects of Territorial Ethics Committee, it has forgotten to define some critical aspect as the different deadline by which ECs must present their opinion on clinical trials. Moreover, other problems arose from the need by Ethics Committee Members to achieve specific competences and delay of presenting trials evaluation in these institutes where ethical dilemmas had not originally arisen⁵.

In the last few years in the EU, the representatives of the academic world of the RECs and of the pharmaceutical industries have started a revision of the Directive 2001/20.

The aim was to achieve true harmonization between the RECs of different Member States, in the definition of roles for the ECs and the competent authorities to decide for the authorization to conduct the clinical trial. This objective was apparently achieved by the European Parliament and the Council with the recent approval of the new EU Regulation 536/2014 which replaced Directive 2001/20.

One of the proposals advanced and adopted by the new EU Regulation was to provide a single Authority (National Ethical Committee) competent for each trial throughout the territory of EU competence. This centralization of approval for European clinical trials was considered essential to simplify and streamline the review process.

The new European Regulation 536/2014 doesn't interfere with the internal organization of Territorial Ethics Committees, which remains of competence of individual Member States. Indeed, the real objective of new EU Regulation 536/2014 is directed to facilitate clinical protocol approval and impose clear deadline for drugs protocol evaluations. In the light of this EU provision, the centralized authorization procedures will make a significant speed up of clinical trials evaluation.

Italy is one of the Member States, which do not have a national Authority. This provision of a National Authority able to evaluation on ethical aspects of clinical trials into the Italian Agency of Drugs could produce same worries on the correct place chosen for it by the Italian Government.

These concerns have been expressed by many experts in the evaluation of experimental protocols for human use. It must be stressed, however, that the problem of a conflict of interests apparently seems to be mitigated by the provision, in Article 2, of an annual periodic self-certification, to which the member of National Authority for Coordination will have duty to produce annually and in which "they will must confirm that they are exempt from any undue influence and that they have no financial or personal interests that could potentially compromise the impartiality of the experimentation"⁶.

Other perplexities emerge in the Italian landscape, in the light of the new Law, such as the excessive reduction of the Territorial Ethics Committees, a reduction that has not been foreseen or imposed by European legislation; or how this reduction could seriously endanger the ethical evaluation of the experimental protocol on medical product for human use⁷. In fact, the idea seems increasingly to be established that a separation between ethical evaluation and the purely scientific evaluation of the protocol can facilitate and speed up its approval/rejection. In reality, the two evaluations cannot be separated, because this separation would fail the deeper sense reason why the Ethical Committees were initially created and because some ethical issues cannot be studied without taking into account their social context.

This National Authority, according to the regulation has an effect only on ethical evaluation of pharmacological, multicentric, and international research protocols. Therefore, the ethical evaluation of not pharmacological experiments (devices, surgical techniques, and other not pharmacological

interventional or not profit observational studies) remains uncovered, and therefore, a legislative intervention is necessary with the aim to regulate this particular clinical trials. It is desirable, to this scope, that the Territorial Ethics Committees can be maintained to provide public guarantees of the protection of human subjects.

Conflict of interest

The authors declare no conflicts of interest.

References

- 1) RICCI G, PIRILLO I, CAMPANOZZI L. The National Ethics Committee: a truly valuable asset for clinical trials? *Eur Rev Med Pharmacol Sci* 2017; 21: 3339-3340.
- 2) Carta di Napoli per la Tutela della Persona nelle Sperimentazioni Cliniche Giugno 2017. http://www.sanita24.ilssole24ore.com/pdf2010/Editrice/ILSOLE24ORE/QUOTIDIANO_SANITA/Online/_Oggetti_Correlati/Documenti/2017/06/15/carta_di_Napoli.pdf?uuid=AEmmAUeB accesso del July 1, 2017 accesso del March 3, 2018.
- 3) Italian National Bioethics Committee, Guidelines for Ethics Committees in Italy, 13th July 2001. http://bioetica.governo.it/media/170664/p50_2001_orientamenti-comitati-et_it.pdf accesso del February 16, 2018.
- 4) MINACORI R, REFOLO P, SACCHINI D, SPAGNOLO AG. Research ethics committees and clinical research in Italy: where are we going? *Eur Rev Med Pharmacol Sci* 2015; 19: 481-485.
- 5) RICCI G, CANNOVO N. The importance of the training of Ethics Committee Members. *Med Law* 2009; 28: 649-659.
- 6) DECRETO LEGISLATIVO 22 dicembre 2017, n. 220, Norme in materia di consenso informato e di disposizioni anticipate di trattamento. <http://www.gazzettaufficiale.it/eli/gu/2018/01/16/12/sg/pdf> accesso del February 16, 2018.
- 7) SPAGNOLO AG. Verso lo smantellamento dei Comitati Etici? *Medicina e Morale* 2015/2: 219-226.

A.G. Spagnolo, E. Midolo

Institute of Bioethics and Medical Humanities (IBioMedH),
Fondazione Policlinico A. Gemelli IRCCS - Università Cattolica Sacro Cuore, Rome, Italy